

2017 ESC Pocket Guidelines

Committee for
Practice Guidelines

DAPT

Focused Update on
Dual Antiplatelet
Therapy in Coronary
Artery Disease



ESC

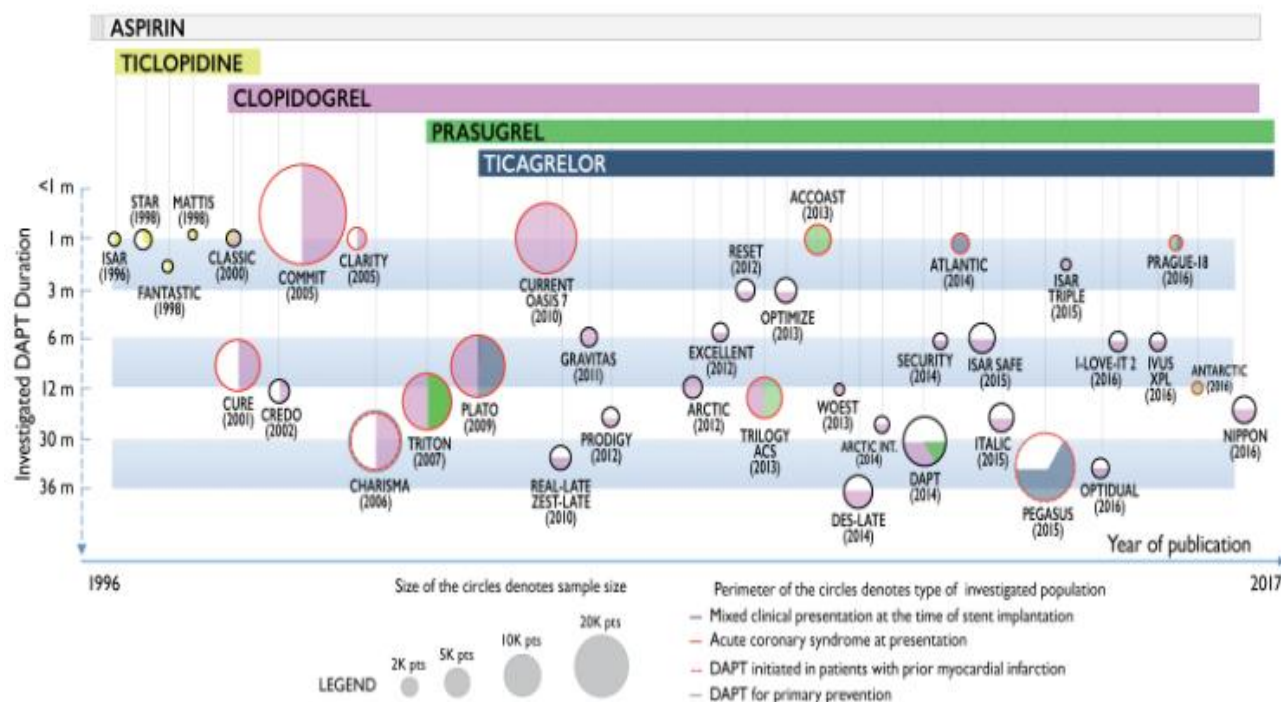
European Society
of Cardiology

www.escardio.org/guidelines

Based on population estimates from 2015, in the region of 1 400 000 and 2 200 000 patients per year may have an indication for **DAPT** after coronary intervention or myocardial infarction (MI), respectively in Europe.

In 2017, it is the 21st anniversary of the publication of the first randomized clinical trial establishing the superiority of **DAPT** over anticoagulant therapy among patients undergoing percutaneous coronary intervention (PCI) (Figure 1). Based on over 35 randomized clinical trials, including more than 225 000 patients, **DAPT** is among the most intensively investigated treatment options in the field of cardiovascular medicine (Figure 1).

Figure 1 History of dual antiplatelet therapy (DAPT) in patients with coronary artery disease



The size of the circles denotes sample size. The colours of perimeters identify the type of included patient populations within each study. The colours within each circle identify the antiplatelet agent(s) investigated. Head-to-head studies comparing similar durations of two different antiplatelet strategies are shown with a vertical line, whereas those investigating different treatment durations are shown with a horizontal line. Studies investigating different treatment strategies or regimens and not treatment durations or type (e.g. pre-treatment in ACCOAST, tailored therapy in GRAVITAS, double dose of clopidogrel in CURRENT OASIS 7, etc.) are represented with a single colour indicating the P2Y₁₂ inhibitor, which was tested on top of aspirin.

< DAPT duration tools and recommendations >

Risk scores

Given the trade-off between ischaemic vs. bleeding risks for any given **DAPT** duration, the use of scores might prove useful to tailor **DAPT** duration in order to maximize ischaemic protection and minimize bleeding risks in the individual patient. The use of risk scores, which were specifically designed to guide and inform decision-making on **DAPT** duration, should be prioritized over other available risk scores (Table 3).

The table below provides an overview for the risk scores, which have been validated for dual antiplatelet therapy duration decision-making

Table 3 Risk scores validated for dual antiplatelet therapy duration decision making

PRECISE-DAPT score																									
Time of use	At the time of coronary stenting																								
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)																								
Score calculation ^a	<p>The nomogram consists of six horizontal scales. From top to bottom: 1. HB: values ≥12, 11-5, 11, 10-5, ≤10. 2. WBC: values ≤5, 8, 10, 12, 14, 16, 18, ≥20. 3. Age: values ≤50, 60, 70, 80, ≥90. 4. CrCl: values ≥100, 80, 60, 40, 20, 0. 5. Prior Bleeding: a line from 'No' to 'Yes'. 6. Score Points: a vertical axis from 0 to 30 in increments of 2.</p>																								
Score range	0 to 100 points																								
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT																								
Calculator	www.precisedaptscore.com																								
DAPT score																									
Time of use	After 12 months of uneventful DAPT																								
DAPT duration strategies assessed	Standard DAPT (12 months) vs. Long DAPT (30 months)																								
Score calculation ^a	<table> <tr> <td>Age</td><td></td></tr> <tr> <td>≥75</td><td>–2 pt</td></tr> <tr> <td>65 to <75</td><td>–1 pt</td></tr> <tr> <td><65</td><td>0 pt</td></tr> <tr> <td>Cigarette smoking</td><td>+1 pt</td></tr> <tr> <td>Diabetes mellitus</td><td>+1 pt</td></tr> <tr> <td>MI at presentation</td><td>+1 pt</td></tr> <tr> <td>Prior PCI or prior MI</td><td>+1 pt</td></tr> <tr> <td>Paclitaxel-eluting stent</td><td>+1 pt</td></tr> <tr> <td>Stent diameter <3 mm</td><td>+1 pt</td></tr> <tr> <td>CHF or LVEF <30%</td><td>+2 pt</td></tr> <tr> <td>Vein graft stent</td><td>+2 pt</td></tr> </table>	Age		≥75	–2 pt	65 to <75	–1 pt	<65	0 pt	Cigarette smoking	+1 pt	Diabetes mellitus	+1 pt	MI at presentation	+1 pt	Prior PCI or prior MI	+1 pt	Paclitaxel-eluting stent	+1 pt	Stent diameter <3 mm	+1 pt	CHF or LVEF <30%	+2 pt	Vein graft stent	+2 pt
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Score range	–2 to 10 points																								
Decision making cut-off suggested	Score ≥2 → Long DAPT Score <2 → Standard DAPT																								
Calculator	www.daptstudy.org																								

PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications

In patients undergoing Stent implantation and subsequent Dual Anti Platelet Therapy; WBC = white blood cell count.

^aFor the PRECISE-DAPT score use the score nomogram: mark patient's value for each of the five clinical variables of the score and draw a vertical line to the 'Point' axis to determine the number of points obtained for each clinical variable. Then summate the points obtained for each clinical variable to the total score.

The table below provides a recommendation on the use of risk scores as guidance for the duration of dual antiplatelet therapy.

Recommendations for the use of risk scores as guidance for the duration of dual antiplatelet therapy

Recommendation	Class ^a	Level ^b
The use of risk scores designed to evaluate the benefits and risks of different DAPT durations ^c may be considered.	IIb	A

DAPT = dual antiplatelet therapy.

^aClass of recommendation.

^bLevel of evidence.

^cThe [DAPT](#) and [PRECISE-DAPT](#) scores are those currently fulfilling these requirements.

Recommendations on P2Y₁₂ inhibitor selection and timing

Recommendations	Class ^a	Level ^b
In patients with ACS , ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin ^c is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contra-indications ^c .	I	B
In patients with ACS undergoing PCI , prasugrel (60 mg loading dose, 10 mg daily dose) on top of aspirin is recommended for P2Y ₁₂ inhibitor-naïve patients with NSTE-ACS or initially conservatively managed STEMI if indication for PCI is established, or in STEMI patients undergoing immediate coronary catheterization unless there is a high-risk of life-threatening bleeding or other contra-indications ^c .	I	B
Pre-treatment with a P2Y ₁₂ inhibitor is generally recommended in patients in whom coronary anatomy is known and the decision to proceed to PCI is made as well as in patients with STEMI .	I	A
In patients with NSTE-ACS undergoing invasive management, ticagrelor administration (180 mg loading dose, 90 mg twice daily), or clopidogrel (600 mg loading dose, 75 mg daily dose) if ticagrelor is not an option, should be considered as soon as the diagnosis is established.	IIa	C
In patients with stable CAD pre-treatment with clopidogrel may be considered if the probability of PCI is high.	IIb	C

Clopidogrel (600 mg loading dose, 75 mg daily dose) on top of aspirin is recommended in stable CAD patients undergoing coronary stent implantation and in ACS patients who cannot receive ticagrelor or prasugrel, including those with prior intracranial bleeding or indication for OAC .	I	A
Clopidogrel (300 mg loading dose in patients aged ≤75, 75 mg daily dose) is recommended on top of aspirin in STEMI patients receiving thrombolysis.	I	A
Ticagrelor or prasugrel on top of aspirin may be considered instead of clopidogrel in stable CAD patients undergoing PCI , taking into account the ischaemic (e.g. high SYNTAX score, prior stent thrombosis, location and number of implanted stents) and bleeding (e.g. according to PRECISE-DAPT) risks.	IIb	C
In NSTEMI-ACS patients in whom coronary anatomy is not known, it is not recommended to administer prasugrel.	III	B

ACS = acute coronary syndrome; CAD = coronary artery disease; DAPT = dual antiplatelet therapy; NSTEMI-ACS = non-ST-elevation acute coronary syndrome; OAC = oral anticoagulant; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREDicting bleeding Complications In patients undergoing Stent implantation and subsequent Dual Anti Platelet Therapy; STEMI = ST-elevation myocardial infarction; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

^aClass of recommendation - ^bLevel of evidence - ^cContra-indications for ticagrelor: previous intracranial haemorrhage or ongoing bleeds. Contra-indications for prasugrel: previous intracranial haemorrhage, previous ischaemic stroke or transient ischaemic attack or ongoing bleeds; prasugrel is not recommended for patients ≥75 years of age or with a bodyweight <60 kg.

< Measures to minimize bleeding ✎ ☆ >

Recommendations on measures to minimize bleeding while on dual antiplatelet therapy		
Recommendations	Class ^a	Level ^b
Radial over femoral access is recommended for coronary angiography and PCI if performed by an expert radial operator.	I	A
In patients treated with DAPT , a daily aspirin dose of 75–100 mg is recommended.	I	A
A PPI in combination with DAPT is recommended. ^c	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended.	III	A

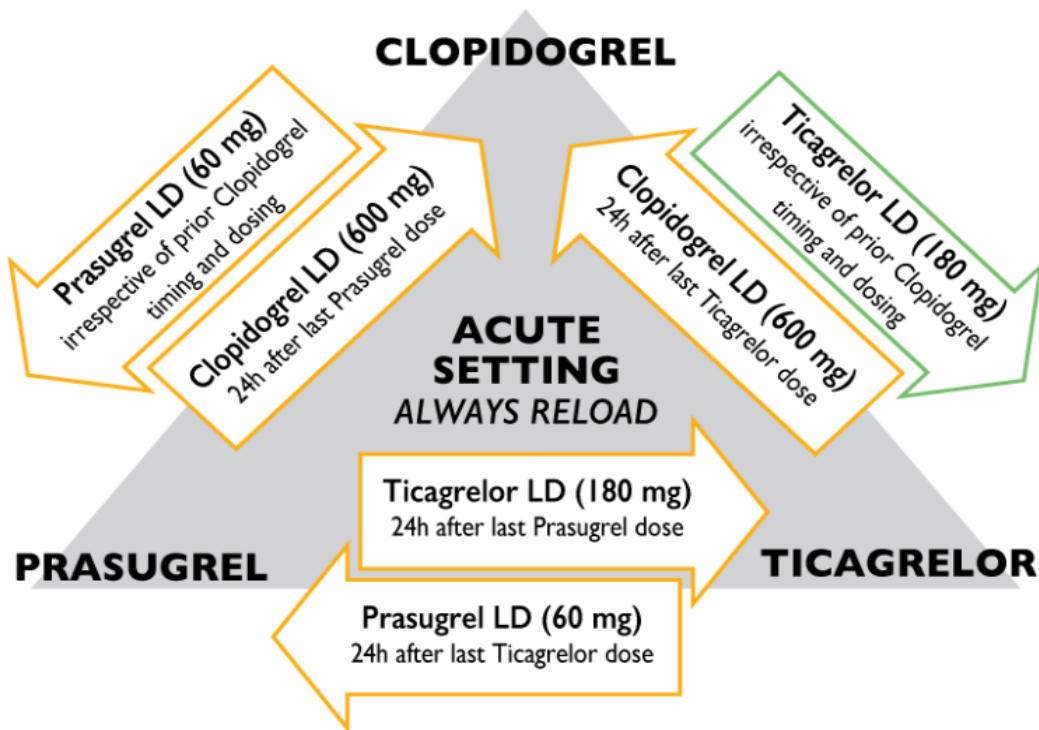
DAPT = dual antiplatelet therapy; PCI = percutaneous coronary intervention; PPI proton pump inhibitor.

^aClass of recommendation - ^bLevel of evidence - ^cWhile the evidence that a PPI does not increase the risk of cardiovascular events was generated with omeprazole, based on drug-drug interaction studies, omeprazole and esomeprazole would appear to have the highest propensity for clinically relevant interactions, while pantoprazole and rabeprazole have the lowest.

Recommendations for switching between oral P2Y ₁₂ inhibitors		
Recommendations	Class ^a	Level ^b
In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contra-indications to ticagrelor exist. ^c	I	B
Additional switching between oral P2Y ₁₂ inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.	IIb	C

ACS = acute coronary syndrome.
^aClass of recommendation - ^bLevel of evidence.
^cContra-indications for ticagrelor: previous intracranial haemorrhage or ongoing bleeds.

Figure 2 Algorithm for switching between oral P2Y₁₂ inhibitors in the acute setting

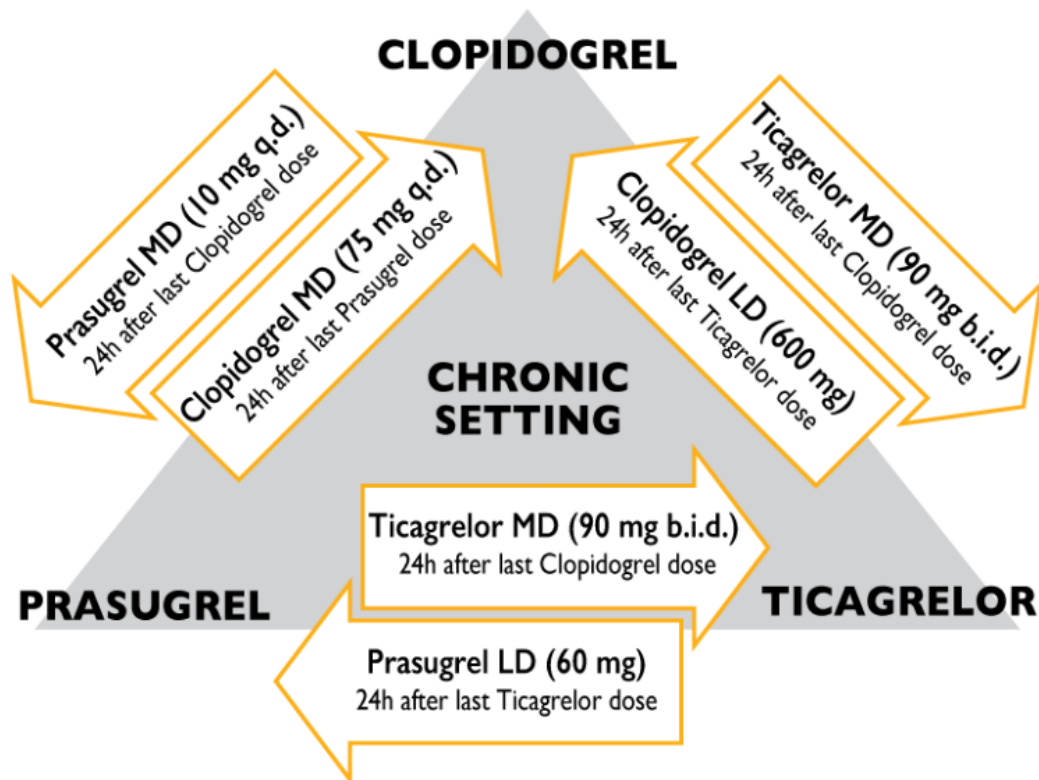


LD = loading dose; MD = maintenance dose

Colour-coding refers to the ESC class of recommendation (green = Class I; orange = Class IIb).

The green arrow from clopidogrel to ticagrelor highlights the only switching algorithm for which outcome data are available in patients with acute coronary syndrome. No outcome data (orange arrows) are available for all other switching algorithms. Acute setting is considered as a switching occurring during hospitalization.

Figure 2bis Algorithm for switching between oral P2Y₁₂ inhibitors in the chronic setting



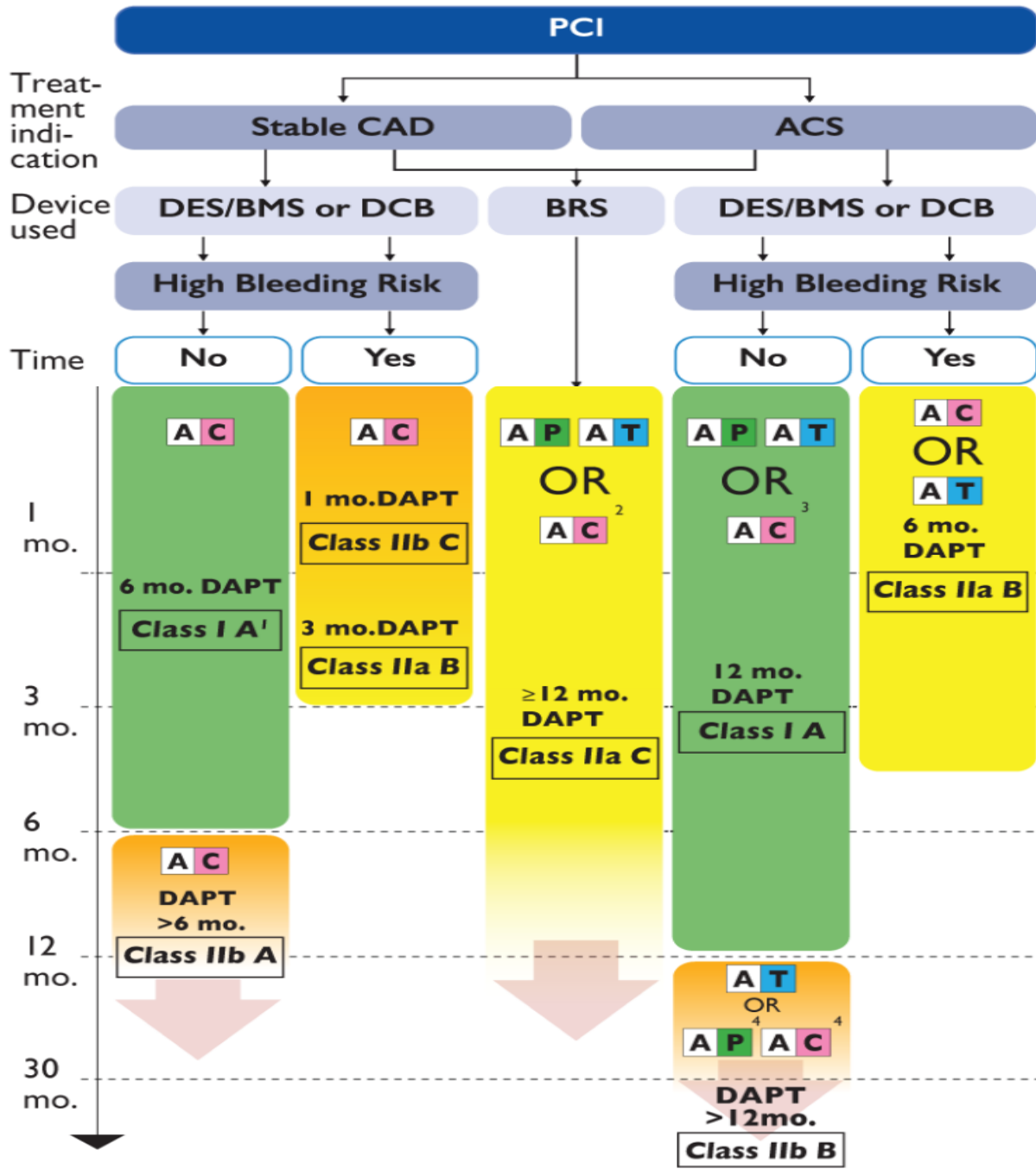
LD = loading dose; MD = maintenance dose

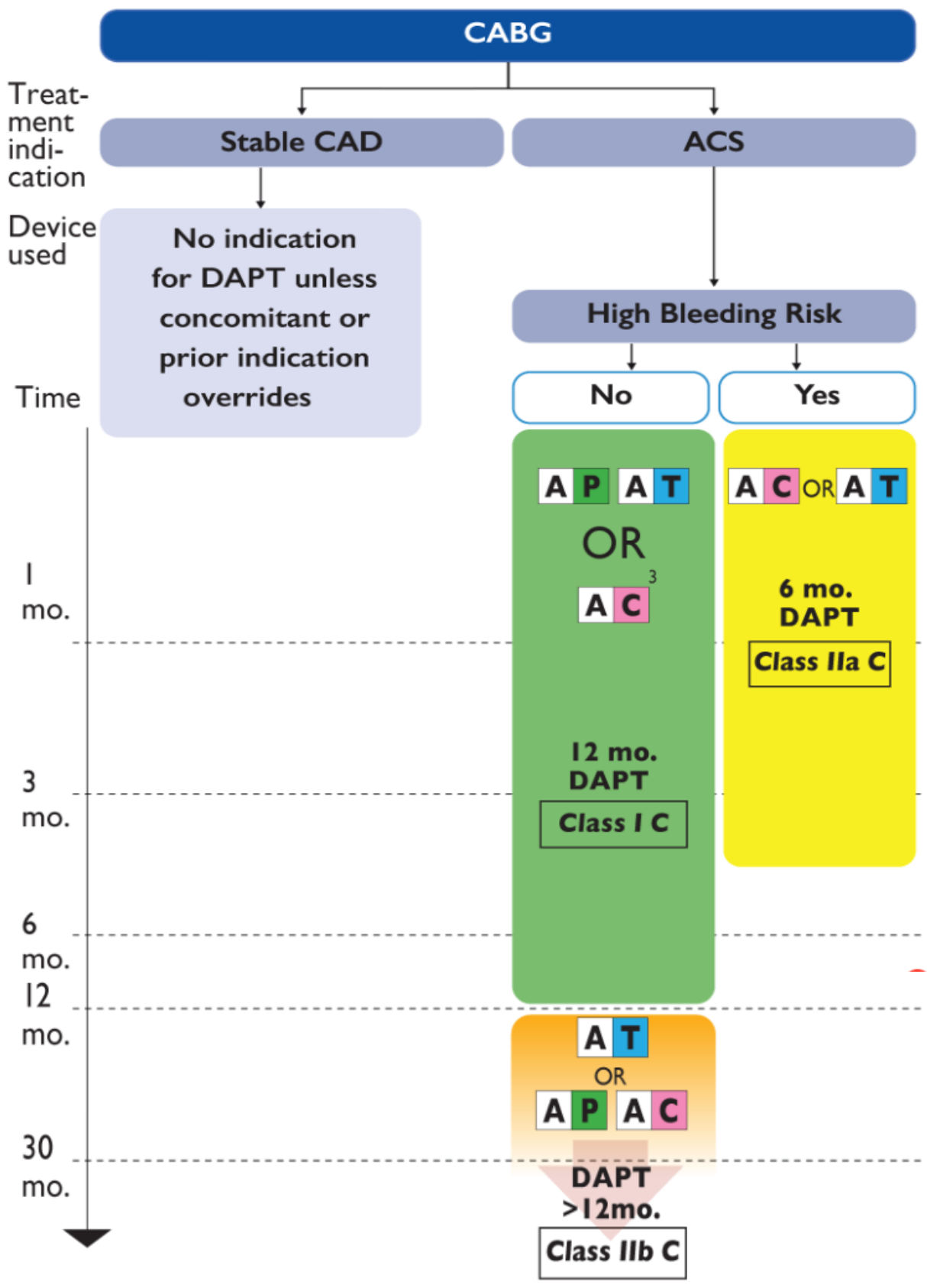
Colour-coding refers to the ESC class of recommendation (orange = Class IIb).

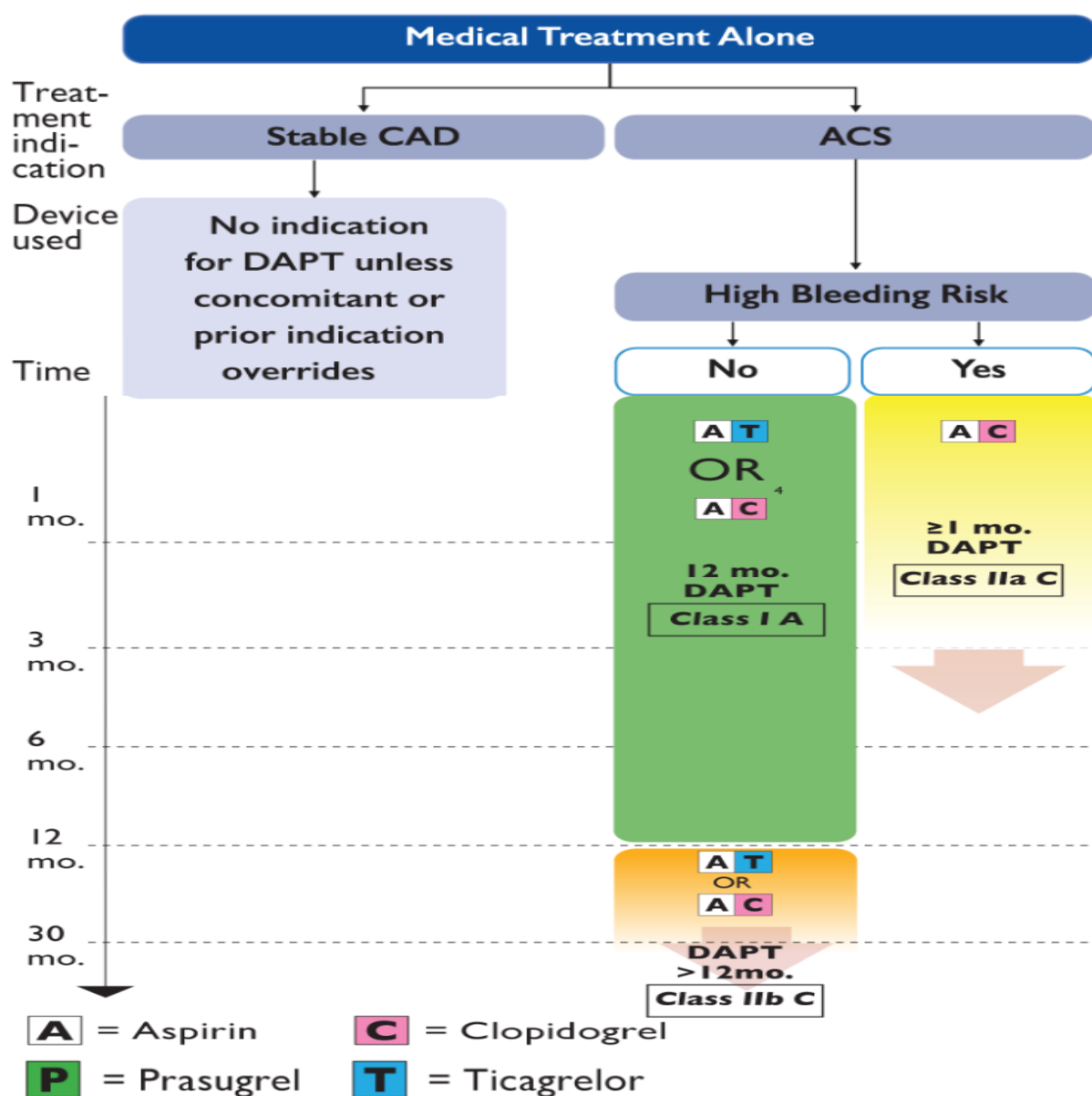
The green arrow from clopidogrel to ticagrelor highlights the only switching algorithm for which outcome data are available in patients with acute coronary syndrome. No outcome data (orange arrows) are available for all other switching algorithms.

An overview of recommendations endorsed by these guidelines regarding [DAPT](#) duration after [PCI](#), as well as after [CABG](#) or in medically managed [ACS](#) patients, is provided in Figure 3 (see below).

Figure 3 Algorithm for dual antiplatelet therapy (DAPT) in patients with coronary artery disease. High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥ 25).







ACS = acute coronary syndrome; BMS = bare-metal stent; BRS = biore-sorbable vascular scaffold; CABG = coronary artery bypass graft ; DCB = drug-coated balloon; DES = drug-eluting stent; PCI = percutaneous coronary intervention; Stable CAD= stable coronary artery disease.

High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥25).

Colour-coding refers to the ESC Classes of Recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).

Treatments presented within the same line are sorted in alphabetic order, no preferential recommendation unless clearly stated otherwise.

¹After PCI with DCB 6 mo. DAPT should be considered (Class IIa B).

²if patient presents with Stable CAD or, in case of ACS, is not eligible for a treatment with prasugrel or ticagrelor.

³if patient is not eligible for a treatment with prasugrel or ticagrelor.

⁴if patient is not eligible for a treatment with ticagrelor.

Recommendations on dual antiplatelet therapy duration and related stent choices in patients with stable coronary artery disease treated with percutaneous coronary intervention

Recommendations	Class ^a	Level ^b
In patients with stable CAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type. ^c	I	A
Irrespective of the intended DAPT duration, DES is the preferred treatment option. ^c	I	A
In patients with stable CAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥ 25), DAPT for 3 months should be considered. ^d	IIa	B
In patients with stable CAD treated with drug-coated balloon, DAPT for 6 months should be considered.	IIa	B
In patients with stable CAD treated with biore-sorbable vascular scaffolds, DAPT for at least 12 months should be considered.	IIa	C
In patients with stable CAD who have tolerated DAPT without a bleeding complication and who are at low bleeding but high thrombotic risk, continuation of DAPT with clopidogrel for >6 months and up to ≤ 30 months may be considered.	IIb	A
In patients with stable CAD in whom 3-month DAPT poses safety concerns, DAPT for 1 month ^e may be considered.	IIb	C

CAD = coronary artery disease; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; PRECISE-DAPT= PREdicting bleeding Complications In patients undergoing Stent implantation and subSEquent Dual Anti Platelet Therapy.

^aClass of recommendation.

^bLevel of evidence.

^cThese recommendations refer to stents which are supported by large-scale randomized trials with clinical endpoint evaluation leading to unconditional CE-mark as detailed in Byrne *et al.* (see Full Text at www.escardio.org/guidelines).

^dThe evidence supporting this recommendation comes from two studies where zotarolimus-eluting Endeavour sprint stent has been investigated in conjunction with a 3-month [DAPT](#) regimen.

^e1-month [DAPT](#) following implantation of zotarolimus-eluting Endeavour sprint stent or drug coated stent reduced risks of re-intervention, myocardial infarction and inconsistently of stent thrombosis compared to bare-metal stent under similar [DAPT](#) duration. It is unclear if this evidence applies to other contemporary [DES](#).

Recommendations on dual antiplatelet therapy duration in patients with acute coronary syndrome treated with percutaneous coronary intervention

Recommendations	Class ^a	Level ^b
In patients with ACS treated with coronary stent implantation, DAPT with a P2Y ₁₂ inhibitor on top of aspirin is recommended for 12 months unless there are contra-indications such as excessive risk of bleeding (e.g. PRECISE-DAPT ≥ 25).	I	A
In patients with ACS and stent implantation who are at high-risk of bleeding (e.g. PRECISE-DAPT ≥ 25), discontinuation of P2Y ₁₂ inhibitor therapy after 6 months should be considered.	IIa	B
In patients with ACS treated with bioresorbable vascular scaffolds, DAPT for at least 12 months should be considered.	IIa	C
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered.	IIb	A
In patients with MI and high ischaemic risk ^c who have tolerated DAPT without a bleeding complication, ticagrelor 60 mg b.i.d. for longer than 12 months on top of aspirin may be preferred over clopidogrel or prasugrel.	IIb	B

ACS = acute coronary syndrome; b.i.d. = bis in die; DAPT = dual antiplatelet therapy. PRECISE-DAPT= PREdicting bleeding Complications In patients undergoing Stent implantation and subSEquent Dual Anti Platelet Therapy.

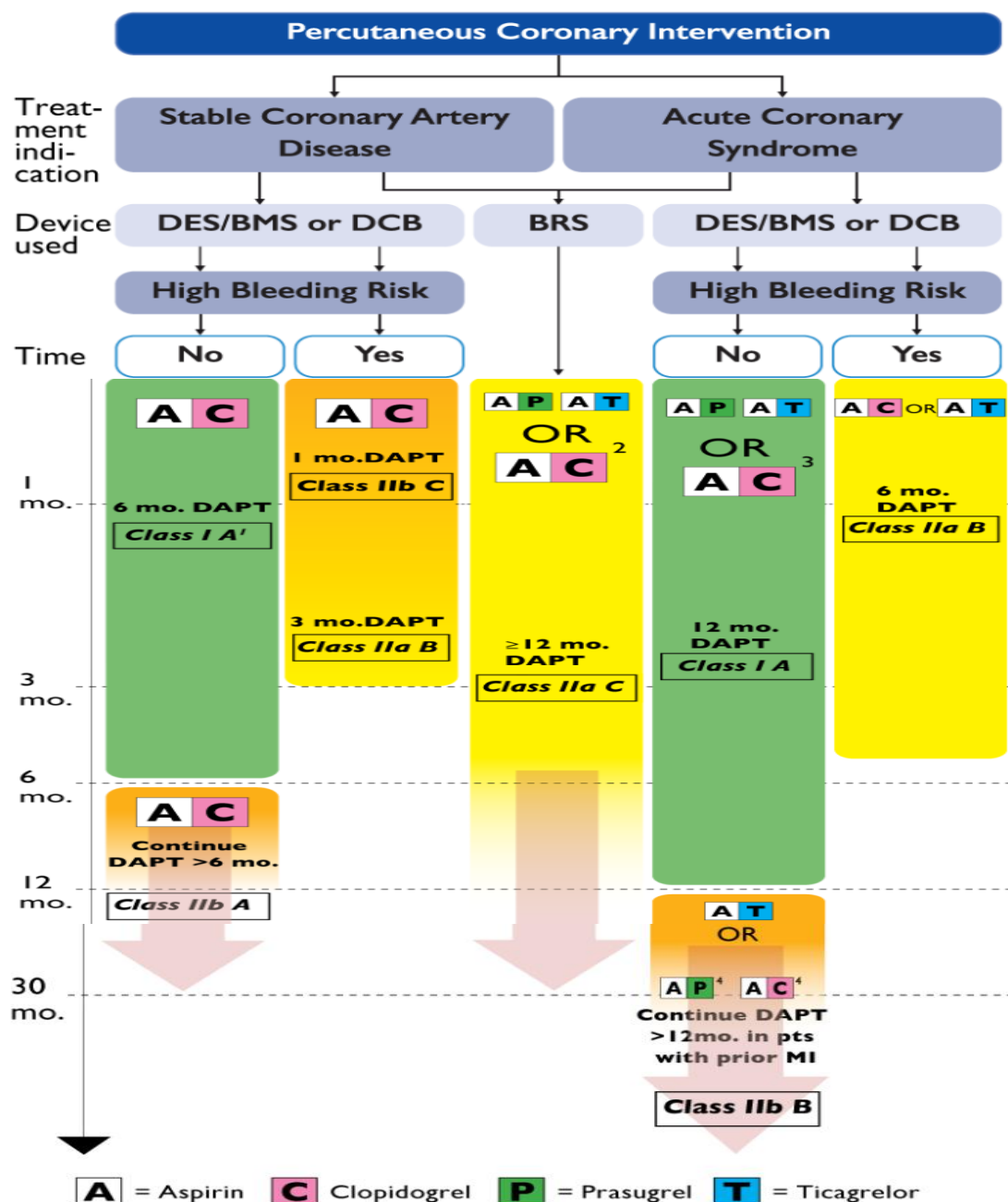
^aClass of recommendation.

^bLevel of evidence.

^cDefined as at least ≥50 years of age, and one or more of the following additional high-risk features: age of 65 years or older, diabetes mellitus requiring medication, a second prior spontaneous myocardial infarction, multivessel coronary artery disease, or chronic renal dysfunction, defined as an estimated creatinine clearance <60 mL per minute.

These recommendations refer to stents that are supported by large-scale randomized trials with clinical endpoint evaluation leading to unconditional CE mark, as detailed in Byrne et al. (see Full Text at www.escardio.org/guidelines)

Figure 4 Algorithm for dual antiplatelet therapy (DAPT) in patients treated with percutaneous coronary intervention.



ACS = acute coronary syndrome; BMS = bare-metal stent; BRS = bioresorbable vascular scaffold; CABG = coronary artery bypass graft surgery; DCB = percutaneous coronary intervention; Stable CAD = stable coronary artery disease. High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥ 25).

Colour-coding refers to the ESC Classes of Recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).

Treatments presented within the same line are sorted in alphabetic order, no preferential recommendation unless clearly stated otherwise.

¹After PCI with DCB 6 mo. DAPT should be considered (Class IIa B).

²if patient presents with SCAD or, in case of ACS, is not eligible for a treatment with prasugrel or ticagrelor.

³if patient is not eligible for a treatment with prasugrel or ticagrelor.

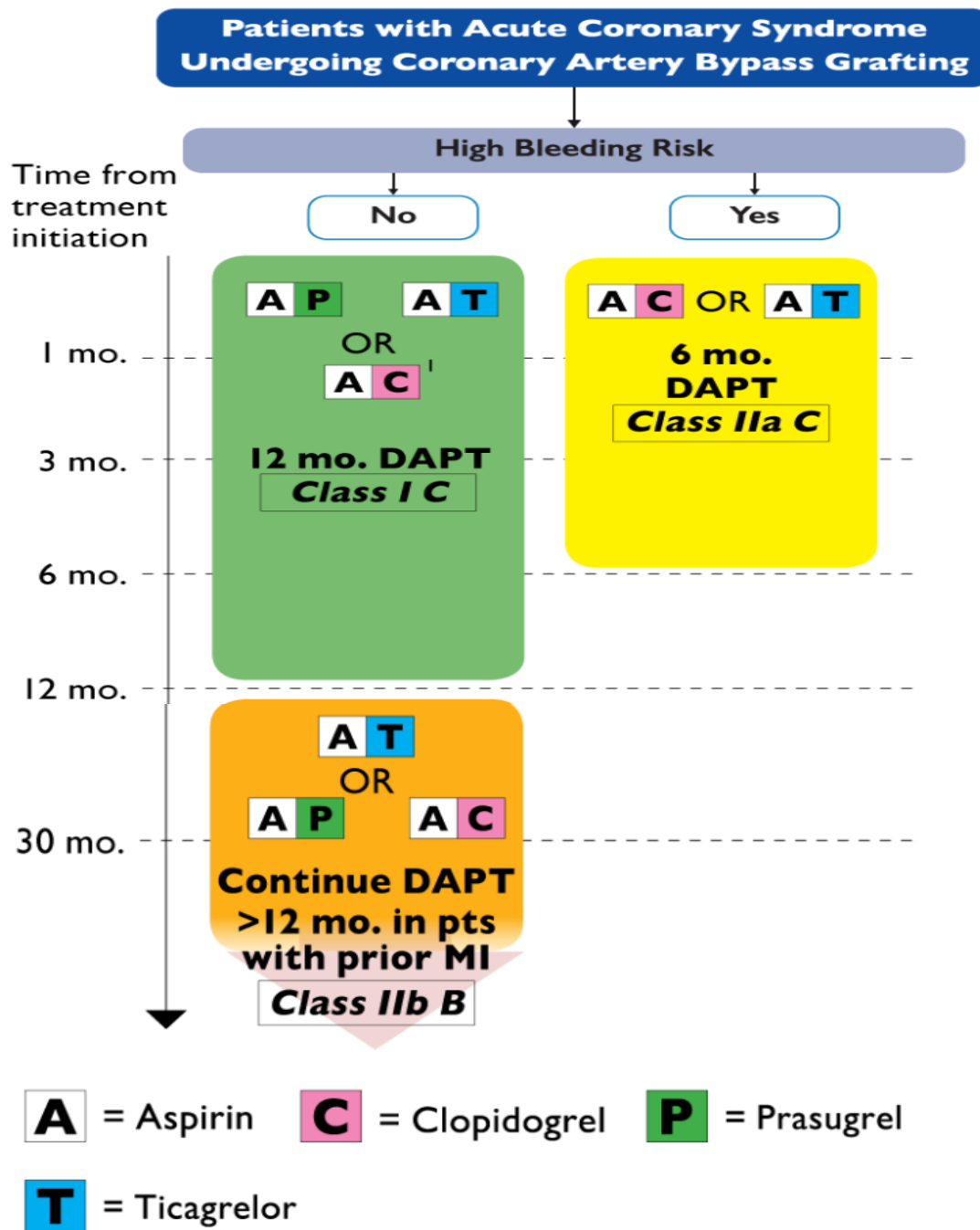
⁴if patient is not eligible for a treatment with ticagrelor.

Recommendations on dual antiplatelet therapy in patients treated with cardiac surgery with stable or unstable coronary artery disease

Recommendations	Class ^a	Level ^b
It is recommended that the Heart Team estimates the individual bleeding and ischaemic risks and guide the timing of CABG as well as the anti-thrombotic management.	I	C
In patients on aspirin who need to undergo non-emergent cardiac surgery, it is recommended to continue aspirin at a low daily regimen throughout the peri-operative period.	I	C
In patients treated with DAPT after coronary stent implantation who subsequently undergo cardiac surgery, it is recommended to resume P2Y ₁₂ inhibitor therapy postoperatively as soon as deemed safe so that DAPT continues until the recommended duration of therapy is completed.	I	C
In patients with ACS (NSTEMI-ACS or STEMI) treated with DAPT and undergoing CABG and not requiring long-term OAC therapy, resumption of P2Y ₁₂ inhibitor therapy as soon as deemed safe after surgery and continuation up to 12 months is recommended.	I	C
In patients on P2Y ₁₂ inhibitors who need to undergo non-emergent cardiac surgery, postponing surgery for at least 3 days after discontinuation of ticagrelor, at least 5 days after clopidogrel, and at least 7 days after prasugrel should be considered.	IIa	B
In CABG patients with prior MI who are at high-risk of severe bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of P2Y ₁₂ inhibitor therapy after 6 months should be considered.	IIa	C
Platelet function testing may be considered to guide decisions on timing of cardiac surgery in patients who have recently received P2Y ₁₂ inhibitors.	IIb	B
In patients perceived at high ischaemic risk with prior MI and CABG who have tolerated DAPT without a bleeding complication, treatment with DAPT for longer than 12 and up to 36 months may be considered.	IIb	C

ACS = acute coronary syndrome; CABG = coronary artery bypass graft; DAPT = non-ST-elevation acute coronary syndrome; OAC = oral anticoagulant; PRECISE-DAPT= PREdicting bleeding Complications in patients undergoing Stent implantation and subSequent Dual Anti Platelet Therapy; STEMI = ST-elevation myocardial infarction.

Figure 5 Algorithm for dual antiplatelet therapy (DAPT) in patients with acute coronary syndrome undergoing coronary artery bypass grafting



Treatments presented within the same line are sorted in alphabetic order, no preferential recommendation unless clearly stated otherwise.

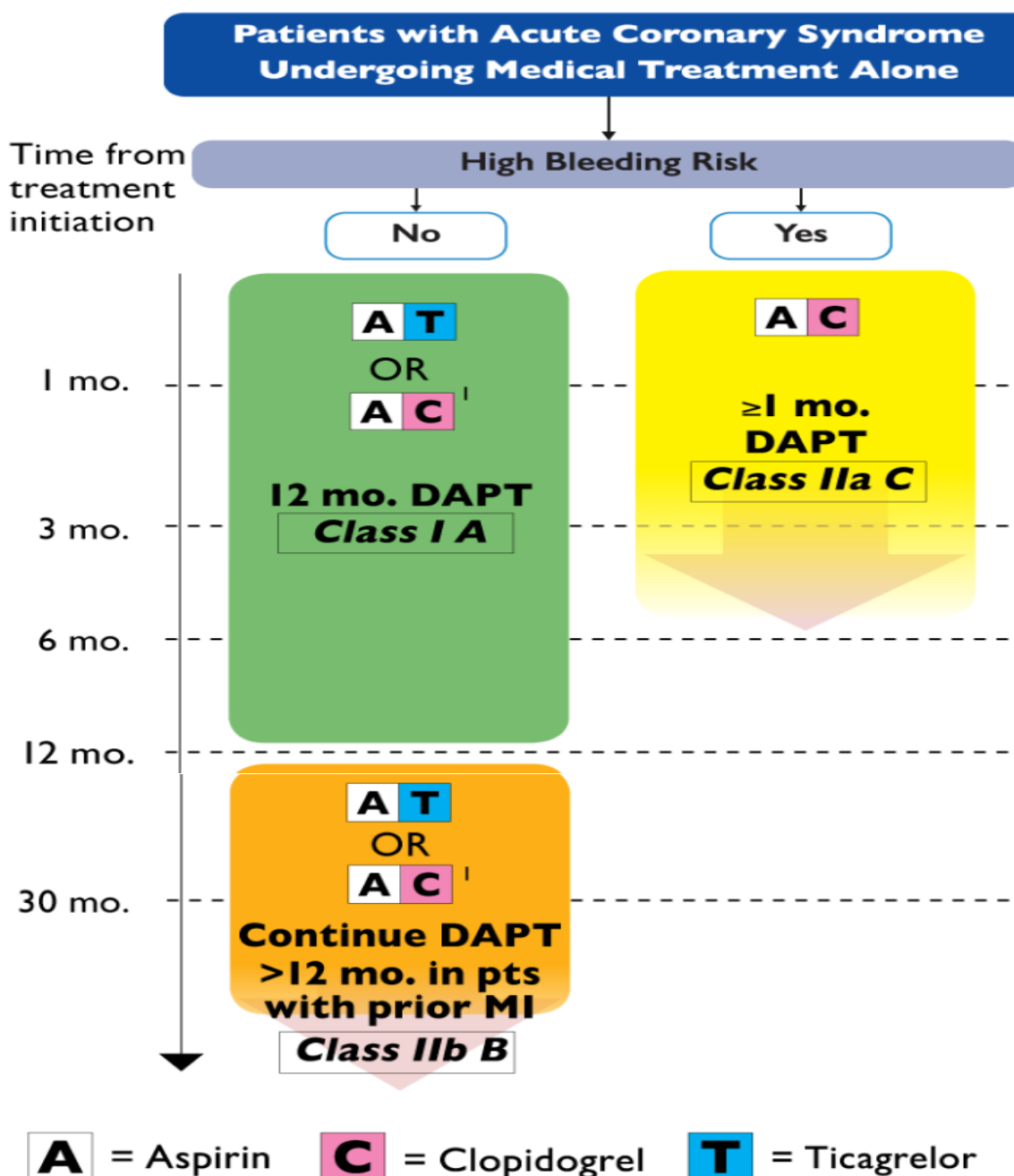
High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. [PRECISE-DAPT](#) score ≥ 25).

Colour-coding refers to the [ESC](#) Classes of Recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).

¹if patient is not eligible for a treatment with prasugrel or ticagrelor.

DAPT in medically managed ACS		
Recommendations		
Recommendations on dual antiplatelet therapy duration in patients with acute coronary syndrome undergoing medical therapy management		
Recommendations	Class ^a	Level ^b
In patients with ACS who are managed with medical therapy alone and treated with DAPT , it is recommended to continue P2Y ₁₂ inhibitor therapy (either ticagrelor or clopidogrel) for 12 months.	I	A
Ticagrelor is recommended over clopidogrel, unless the bleeding risk outweighs the potential ischaemic benefit.	I	B
In patients with medically managed ACS who are at high-risk of bleeding (e.g. PRECISE-DAPT ≥ 25), DAPT for at least 1 month should be considered.	IIa	C
In patients with prior MI at high ischaemic risk ^c who are managed with medical therapy alone and have tolerated DAPT without a bleeding complication, treatment with DAPT in the form of ticagrelor 60 mg b.i.d. on top of aspirin for longer than 12 months and up to 36 months may be considered.	IIb	B
In patients with prior MI not treated with coronary stent implantation who have tolerated DAPT without a bleeding complication and who are not eligible for treatment with ticagrelor, continuation of clopidogrel on top of aspirin for longer than 12 months may be considered.	IIb	C
Prasugrel is not recommended in medically managed ACS patients.	III	B
<p>ACS = acute coronary syndrome; DAPT = dual antiplatelet therapy; MI = myocardial infarction. PRECISE- DAPT= PREdicting bleeding Complications In patients undergoing Stent implantation and subSEquent Dual Anti Platelet Therapy.</p> <p>^aClass of recommendation.</p> <p>^bLevel of evidence.</p> <p>^cDefined as ≥50 years of age, and one or more of the following additional high-risk features: age of 65 years or older, diabetes mellitus requiring medication, a second prior spontaneous myocardial infarction, multivessel coronary artery disease, or chronic renal dysfunction, defined as an estimated creatinine clearance <60 mL per minute.</p>		

Figure 6 Algorithm for dual antiplatelet therapy (DAPT) in patients with acute coronary syndrome undergoing medical management



Treatments presented within the same line are sorted in alphabetic order, no preferential recommendation unless clearly stated otherwise.

High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. [PRECISE-DAPT](#) score ≥ 25).

Colour-coding refers to the ESC Classes of Recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).

¹if patient is not eligible for a treatment with ticagrelor

Strategies to avoid bleeding complications in patients treated with oral anticoagulant are summarised in the table below.

Table 4 Strategies to avoid bleeding complications in patients treated with oral anticoagulant

- Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA₂DS₂-VASc, [ABC](#), HAS-BLED) with a focus on modifiable risk factors.
- Keep triple therapy duration as short as possible; dual therapy after [PCI](#) (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
- Consider the use of [NOACs](#) instead of [VKA](#) when [NOACs](#) are not contra-indicated.
- Consider a target [INR](#) in the lower part of the recommended target range and maximize time in therapeutic range (i.e. >65–70%) when [VKA](#) is used.
- Consider the lower [NOAC](#) regimen tested in approval studies and apply other [NOAC](#) regimens based on drug-specific criteria for drug accumulation.^a
- Clopidogrel is the P2Y₁₂ inhibitor of choice.
- Use low-dose (≤100 mg daily) aspirin.
- Routine use of [PPIs](#).

ABC = Age, Biomarkers, Clinical history; CHA₂DS₂-VASc = Congestive heart failure, Hypertension, Age ≥ 75 years (doubled), Diabetes mellitus, prior Stroke or transient ischaemic attack or thromboembolism (doubled), Vascular disease, Age 65–74 years, Sex category; HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR = non-vitamin-K oral anticoagulant; INR = international normalized ratio; PCI = percutaneous coronary intervention; PPIs = proton pump inhibitors; VKA = vitamin K antagonist.

^aApixaban 5 mg b.i.d. or apixaban 2.5 mg b.i.d. if at least two of the following: age ≥80 years, body weight ≤60 kg or serum creatinine level ≥1.5 mg/dL (133 μmol/L); dabigatran 110 mg b.i.d.; edoxaban 60 mg q.d. or edoxaban 30 mg q.d. if any of the following: creatinine clearance (CrCl) of 30–50 mL/min, body weight ≤60 kg, concomitant use of verapamil or quinidine or dronedarone; rivaroxaban 20 mg q.d. or rivaroxaban 15 mg q.d. if [CrCl](#) 30–49 mL/min.

< DAPT and concomitant OAC >

< Stent-related high ischemic risk features   >

Table 5 High-risk features of stent-driven recurrent ischaemic events

- Prior stent thrombosis on adequate antiplatelet therapy
- Stenting of the last remaining patent coronary artery
- Diffuse multivessel disease especially in diabetic patients
- Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
- At least three stents implanted
- At least three lesions treated
- Bifurcation with two stents implanted
- Total stent length >60 mm
- Treatment of a chronic total occlusion

< DAPT and concomitant OAC >


< Unfavourable pt. profile for OAC & APT   >

Table 6 Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

- Short life expectancy
- Ongoing malignancy
- Poor expected adherence
- Poor mental status
- End stage renal failure
- Advanced age
- Prior major bleeding/prior haemorrhagic stroke
- Chronic alcohol abuse
- Anaemia
- Clinically significant bleeding on dual antithrombotic therapy

Recommendations on dual antiplatelet therapy duration in patients with indication for oral anticoagulation

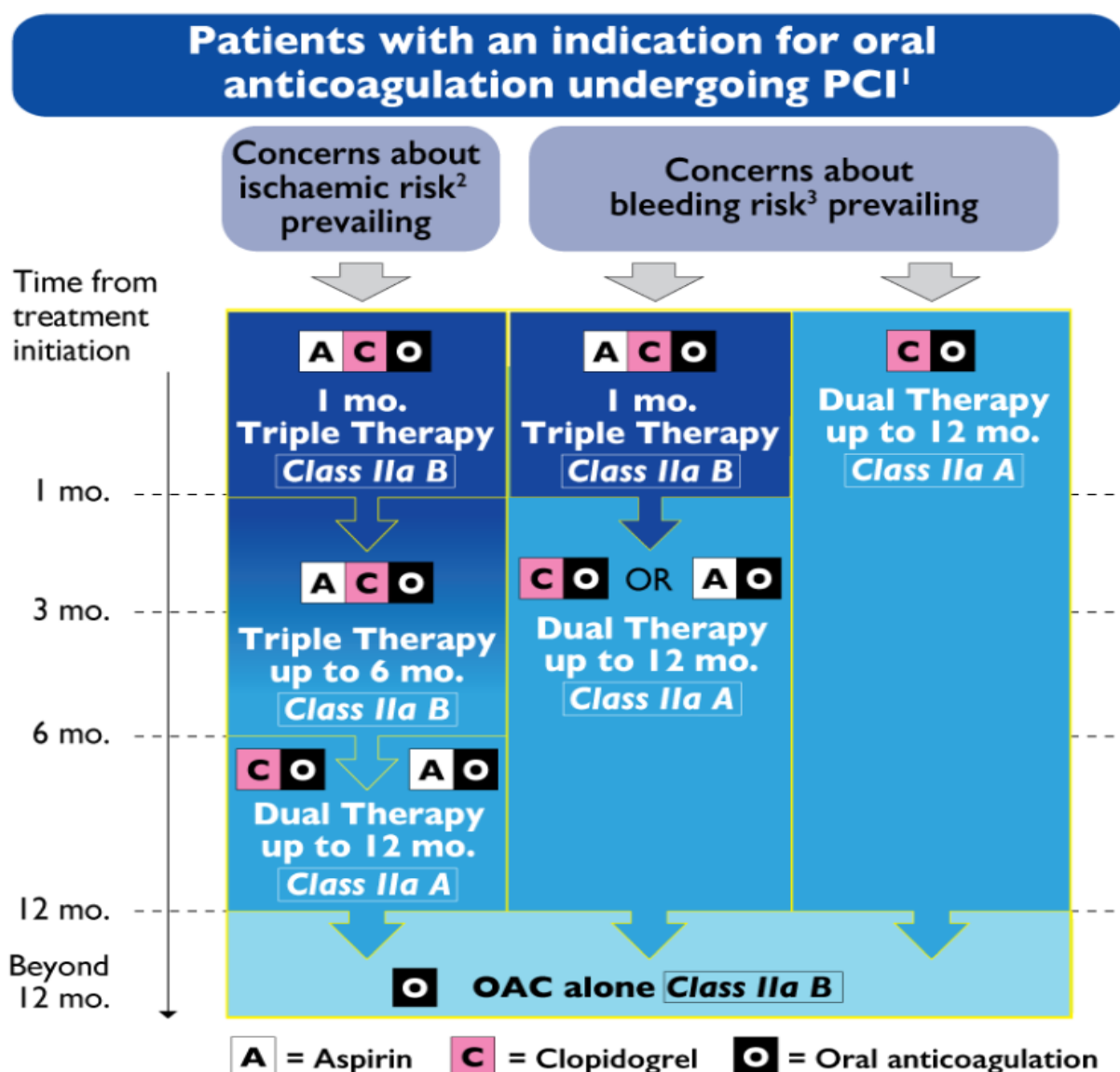
Recommendations	Class ^a	Level ^b
It is recommended to administer periprocedurally aspirin and clopidogrel in patients undergoing coronary stent implantation.	I	C
In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel and OAC should be considered for 1 month, irrespective of the type of stent used.	IIa	B
Triple therapy with aspirin, clopidogrel and OAC for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk.	IIa	B
Dual therapy with clopidogrel 75 mg/day and OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk.	IIa	A
Discontinuation of antiplatelet treatment in patients treated with OAC should be considered at 12 months.	IIa	B
In patients with an indication for VKA in combination with aspirin and/or clopidogrel, the dose intensity of VKA should be carefully regulated with a target INR in the lower part of the recommended target range and a time in the therapeutic range >65–70%.	IIa	B
When a NOAC is used in combination with aspirin and/or clopidogrel, the lowest approved dose effective for stroke prevention tested in AFib trials should be considered. ^c	IIa	C
When rivaroxaban is used in combination with aspirin and/or clopidogrel, rivaroxaban 15 mg q.d. may be used instead of rivaroxaban 20 mg q.d.	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and OAC .	III	C

ACS = acute coronary syndrome; INR = international normalized ratio; OAC = oral anticoagulant; NOAC = non-vitamin K oral anticoagulant; q.d. = *quaque die*; VKA = vitamin K antagonist.

^aClass of recommendation - ^bLevel of evidence.

^cApixaban 5 mg *b.i.d.* or apixaban 2.5 mg *b.i.d.* if at least two of the following: age ≥80 years, body weight ≤60 kg or serum creatinine level ≥1.5 mg/dL (133 μmol/L); dabigatran 110 mg *b.i.d.*; edoxaban 60 mg q.d. or edoxaban 30 mg q.d. if any of the following: creatinine clearance (CrCl) of 30–50 mL/min, body weight ≤60 kg, concomitant use of verapamil or quinidine or dronedarone; rivaroxaban 20 mg q.d. or rivaroxaban 15 mg q.d. if [CrCl](#) 30–49 mL/min.

Figure 7 Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention (PCI)



Colour-coding refers to the number of concomitant antithrombotic medication(s). Triple therapy denotes treatment with DAPT plus oral anticoagulant (OAC). Dual therapy denotes treatment with a single antiplatelet agent (aspirin or clopidogrel) plus OAC.

ABC = age, biomarkers, clinical history; ACS = acute coronary syndrome; mo. = month(s); PCI = percutaneous coronary intervention

¹Periprocedural administration of aspirin and clopidogrel during [PCI](#) is recommended irrespective of the treatment strategy.

²High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction. 3: Bleeding risk can be estimated by [HAS-BLED](#) or [ABC](#) score.

The table below summarizes the recommendations on dual antiplatelet therapy in patients undergoing elective non-cardiac surgery.

Recommendations on dual antiplatelet therapy in patients undergoing elective non-cardiac surgery		
Recommendations	Class ^a	Level ^b
It is recommended to continue aspirin perioperatively if the bleeding risk allows, and to resume the recommended antiplatelet therapy as soon as possible post-operatively.	I	B
After coronary stent implantation, elective surgery requiring discontinuation of the P2Y ₁₂ inhibitor should be considered after 1 month, irrespective of the stent type, if aspirin can be maintained throughout the peri-operative period.	IIa	B
Discontinuation of P2Y ₁₂ inhibitors should be considered at least 3 days before surgery for ticagrelor, at least 5 days for clopidogrel and at least 7 days for prasugrel.	IIa	B
A multidisciplinary expert team should be considered for pre-operative evaluation of patients with an indication for DAPT before elective surgery.	IIa	C
In patients with recent MI or other high ischaemic risk features ^c requiring DAPT , elective surgery may be postponed for up to 6 months.	IIb	C
If both oral antiplatelet agents have to be discontinued perioperatively, a bridging strategy with intravenous antiplatelet agents may be considered, especially if surgery has to be performed within 1 month after stent implantation.	IIb	C
It is not recommended to discontinue DAPT within the first month of treatment in patients undergoing elective non-cardiac surgery.	III	B

Figure 8 Timing for elective non-cardiac surgery in patients treated with dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI)

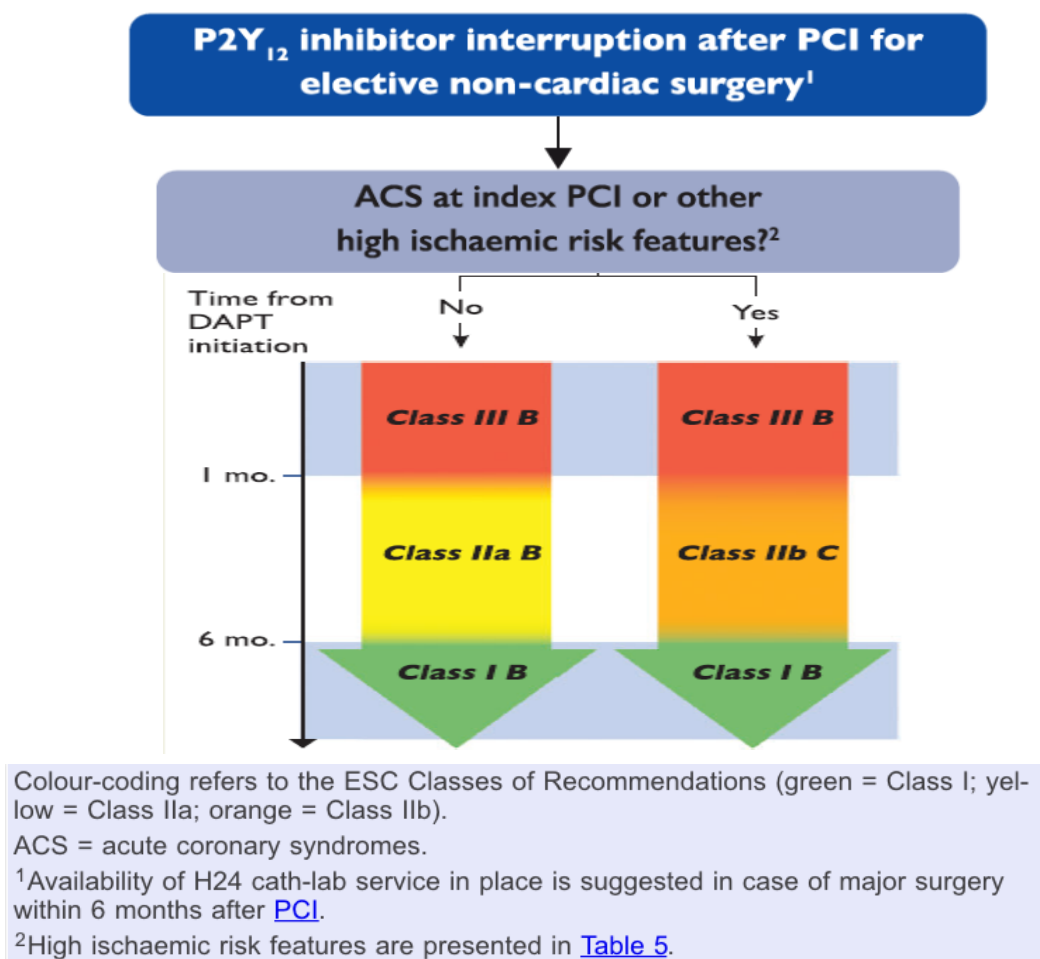
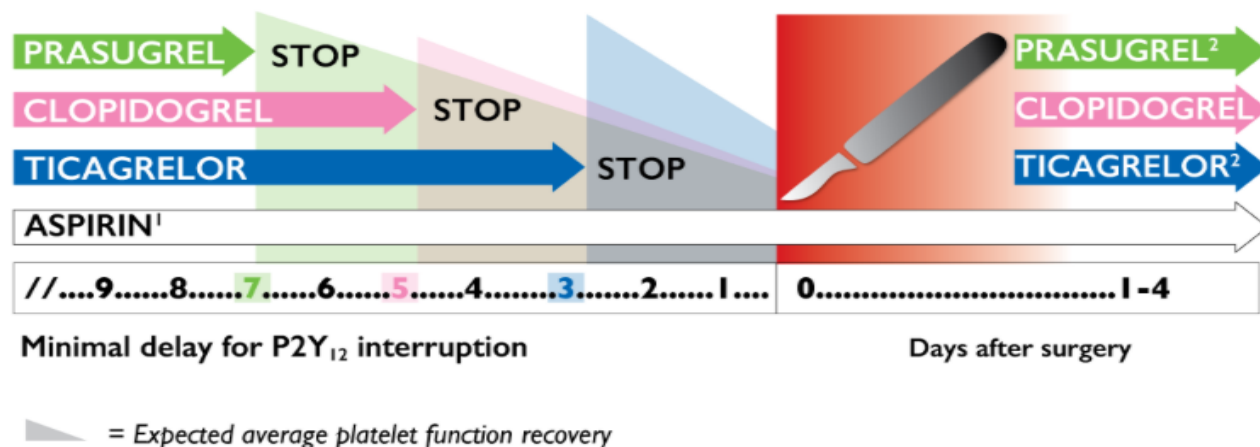


Figure 9 Minimal discontinuation and re-implementation time frames of dual antiplatelet therapy (DAPT) for patients undergoing elective surgery



¹Decision to stop aspirin throughout surgery should be made on a single case basis taking into account the surgical bleeding risk.

²In patients not requiring OAC = oral anticoagulant.

Recommendations related to gender considerations and those for special populations are shown in the table below.

Recommendations on gender considerations and those for special populations		
Recommendations	Class ^a	Level ^b
Similar type and duration of DAPT are recommended in male and female patients.	I	A
It is recommended to reassess the type, dose and duration of DAPT in patients with actionable bleeding complication while on treatment.	I	C
Similar type and duration of DAPT should be considered in patients with and without diabetes mellitus.	IIa	B
Prolonged (i.e. >12 months ^c) DAPT duration should be considered in patients with prior stent thrombosis, especially in the absence of correctable causes (e.g. lack of adherence or correctable mechanical stent-related issues).	IIa	C
Prolonged (i.e. >12 months) DAPT duration may be considered in CAD patients with LEAD .	IIb	B
Prolonged (i.e. >6 months) DAPT duration may be considered in patients who underwent complex PCI . ^d	IIb	B
<p>CAD = coronary artery disease; DAPT = dual antiplatelet therapy; LEAD = lower-extremities artery disease; PCI = percutaneous coronary intervention.</p> <p>^aClass of recommendation.</p> <p>^bLevel of evidence.</p> <p>^cAnd possibly as long as tolerated.</p> <p>^dComplex PCI defined as the composite of ≥ three stents implanted, ≥ three lesions treated, bifurcation with two stents implanted, total stent length >60 mm and chronic total occlusion as target lesion.</p>		

Practical recommendations for the management of bleeding in patients treated with dual antiplatelet therapy with or without concomitant oral anticoagulation are showed in the figure 10.

Bleeding during treatment with dual antiplatelet therapy ± OAC

TRIVIAL BLEEDING

Any bleeding not requiring medical intervention or further evaluation

e.g. skin bruising or ecchymosis, self-resolving epistaxis, minimal conjunctival bleeding

- Continue DAPT
- Consider OAC continuation or skip one single next pill
- Reassure the patient
- Identify and discuss with the patient possible preventive strategies
- Counsel patient on the importance of drug-adherence

MILD BLEEDING

Any bleeding that requires medical attention without requiring hospitalization

e.g. not self resolving epistaxis, moderate conjunctival bleeding, genitourinary or upper/lower gastrointestinal bleeding without significant blood loss, mild haemoptysis

- Continue DAPT
- Consider shortening DAPT duration or switching to less potent P2Y₁₂ inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs
- In case of triple therapy consider downgrading to dual therapy, preferably with clopidogrel and OAC
- Identify and possibly treat concomitant conditions associated with bleeding (e.g. peptic ulcer, haemorrhoidal plexus, neoplasm)
- Add PPI if not previously implemented
- Counsel patient on the importance of drug-adherence

MODERATE BLEEDING

Any bleeding associated with a significant blood loss (>3 g/dL HB) and/or requiring hospitalization, which is haemodynamically stable and not rapidly evolving

e.g. genitourinary, respiratory or upper/lower gastrointestinal bleeding with significant blood loss or requiring transfusion

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y₁₂ inhibitor especially in case of upper GI bleeding
- Reinitiate DAPT as soon as deemed safe
- Consider shortening DAPT duration or switching to less potent P2Y₁₂ inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs
- Consider OAC discontinuation or even reversal until bleeding is controlled, unless very high thrombotic risk (i.e. mechanical heart valves, cardiac assist device, CHA₂DS₂-VASc ≥4)
- Reinitiate treatment within one week if clinically indicated. For Vitamin-K antagonist consider a target INR of 2.0–2.5 unless overriding indication (i.e. mechanical heart valves or cardiac assist device) for NOAC consider the lowest effective dose
- In case of triple therapy consider downgrading to dual therapy, preferably with clopidogrel and OAC
- If patients on dual therapy, consider stopping antiplatelet therapy if deemed safe
- Consider i.v. PPI if GI bleeding occurred
- Identify and possibly treat concomitant conditions associated with bleeding (e.g. peptic ulcer, haemorrhoidal plexus, neoplasm)
- Counsel patient on the importance of drug-adherence

Legend

DAPT management

OAC management

General recommendations

Bleeding during treatment with dual antiplatelet therapy ± OAC

SEVERE BLEEDING

Any bleeding requiring hospitalisation, associated with a severe blood loss (>5 g/dL HB) which is haemodynamically stable and not rapidly evolving

e.g. severe genitourinary, respiratory or upper/lower gastrointestinal bleeding

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y₁₂ inhibitor especially in case of upper GI bleeding
- If bleeding persists despite treatment or treatment is not possible, consider stopping all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y₁₂ inhibitor especially in case of upper GI bleeding
- If DAPT is re-started, consider shortening DAPT duration or switching to less potent P2Y₁₂ inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

- Consider stopping and reversing OAC until bleeding is controlled unless prohibitive thrombotic risk (i.e. mechanical heart valve in mitral position, cardiac assist device)
- Reinitiate treatment within one week if clinically indicated. For vitamin-K antagonists consider a target INR of 2.0–2.5 unless overriding indication (i.e. mechanical heart valves or cardiac assist device) for NOAC consider the lowest effective dose
- If patient on triple therapy consider downgrading to dual therapy with clopidogrel and OAC. If patients on dual therapy, consider stopping antiplatelet therapy if deemed safe

- Consider i.v. PPI if GI bleeding occurred
- RBC transfusion if HB <7-8 g/dL
- Consider platelet transfusion
- Urgent surgical or endoscopic treatment of bleeding source if deemed possible

LIFE-THREATENING BLEEDING

Any severe active bleeding putting patient's life immediately at risk

e.g. massive overt genitourinary, respiratory or upper/lower gastrointestinal bleeding, active intracranial, spinal or intraocular haemorrhage, or any bleeding causing haemodynamic instability

- Immediately discontinue all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y₁₂ inhibitor especially in case of upper GI bleeding

• Stop and reverse OAC

- Fluid replacement if hypotension
- Consider RBC transfusion irrespective of HB values
- Platelet transfusion
- Consider i.v. PPI if GI bleeding occurred
- Urgent surgical or endoscopic treatment of bleeding source if deemed possible

Legend

DAPT management

OAC management

General recommendations

ACS = acute coronary syndrome; CHA₂DS₂-VASc = cardiac failure, hypertension, age ≥ 75 (2 points), diabetes, stroke (2 points)–vascular disease, age 65–74, sex category; DAPT = dual antiplatelet therapy; GI = gastrointestinal; HB = haemoglobin; INR = international normalized ratio; i.v. = intravenous; OAC = oral anticoagulant; NOAC = non-vitamin-K antagonist; PPI = proton pump inhibitor; RBC = red blood cell; SAPT = single antiplatelet therapy.